

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Applicants:	: Lars Terje Holmaas et al.	
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Customer No.	: 36335	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RULE 132 DECLARATION

In accordance with rule 37 CFR 1.112, I, Ole Magne Homestad, do hereby declare that:

I am inventor of said invention and currently reside in Sør-Audnedal, Norway.

Reference is made to the Office Actions dated 11/21/2006, 04/26/2007, 10/29/2007 and 04/14/2008.

In the present N-alkylation step of the synthesis of iohexol 2-methoxyethanol (2-ME) is used as solvent. When we searched for an alternative solvent to 2-ME, we considered the "nearest neighbour" of 2-ME, namely 2-ethoxyethanol. It was impossible to use this solvent due to solubility and selectivity. 1-methoxy-2-propanol (PM) was not considered since it was estimated to be even less polar than 2-ethoxyethanol.

To be able to use a solvent in the alkylation step it is necessary that NaOH is soluble. This is the case for 2-ME. Regarding PM, NaOH was not soluble and hence, it would be impossible to dissolve '541' to obtain alkylation reaction conditions.

At first a modification of PM by adding co-solvents for increasing solubility of NaOH was not considered due to the assumption that such an addition would worsen selectivity of the

reaction. This is true for 2-ME. It was therefore definitely not obvious to pursue this lead any further.

In summary it was not believed that PM was able to substitute 2-ME. This assumption was based on decades of experience with these processes and general chemical knowledge. It was consequently much unexpected that PM turned out to be a suitable replacement for 2-ME.

I declare under penalty of perjury pursuant to the laws of the United States of America that the foregoing is true and correct, and that this declaration was executed by me on 11th July 2008 at Spangereid, Norway.



Ole Magne Hamestad